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10/724,108	12/01/2003	Hideki Thoda	245694USOCONT	3217
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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C. 1940 DUKE STREET ALEXANDRIA, VA 22314				
EXAMINER				
JOKE, MICHELE K				
ART UNIT		PAPER NUMBER		
1636				
NOTIFICATION DATE		DELIVERY MODE		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary

Application No.

10/724,108

Applicant(s)

THODA ET AL.

Examiner

MICHELE K. JOIKE

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 14, 15, 17-21 and 23-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 14, 15, 17-21 and 23-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/S508)
Paper No(s)/Mail Date 7/14/08
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 15, 2008 has been entered.

Receipt is acknowledged of a reply to the previous Office Action, filed April 15, 2008. Claims 1-13, 16 and 22 are canceled. Claims 14, 15, 17-21 and 23-25 were amended. Claims 14, 15, 17-21 and 23-25 are pending and examined. Any rejection of record in the previous Office Action, mailed January 20, 2008 that is not addressed in this action has been withdrawn.

Priority

This application claims benefit to PCT application No. PCT/JP02/05223, filed on May 29, 2002, in a language other than English. Since the instant application is claiming benefit as a continuation of PCT/JP02/05223, PCT/JP02/05223 must be submitted with a certified English translation. Appropriate correction is required. See below.

35 U.S.C. 365 Right of priority; benefit of the filing date of a prior application.

(a) In accordance with the conditions and requirements of subsections (a) through (d) of section 119 of this title, a national application shall be entitled to the right of priority based on a prior filed international application which designated at least one country other than the United States.

(b) In accordance with the conditions and requirements of section 119(a) of this

title and the treaty and the Regulations, an international application designating the United States shall be entitled to the right of priority based on a prior foreign application, or a prior international application designating at least one country other than the United States.

(c) In accordance with the conditions and requirements of section 120 of this title, an international application designating the United States shall be entitled to the benefit of the filing date of a prior national application or a prior international application designating the United States, and a national application shall be entitled to the benefit of the filing date of a prior international application designating the United States. If any claim for the benefit of an earlier filing date is based on a prior international application which designated but did not originate in the United States, the Director may require the filing in the Patent and Trademark Office of a certified copy of such application together with a translation thereof into the English language, if it was filed in another language.

35 U.S.C. 361 Receiving Office.

(a) The Patent and Trademark Office shall act as a Receiving Office for international applications filed by nationals or residents of the United States. In accordance with any agreement made between the United States and another country, the Patent and Trademark Office may also act as a Receiving Office for international applications filed by residents or nationals of such country who are entitled to file international applications.

(b) The Patent and Trademark Office shall perform all acts connected with the discharge of duties required of a Receiving Office, including the collection of international fees and their transmittal to the International Bureau.

(c) International applications filed in the Patent and Trademark Office shall be in the English language.

Response to Arguments Concerning Claim Rejections – 35 USC § 102 (b)

Applicants' arguments filed on March 11, 2008 have been fully considered. The following grounds of traversal are presented:

Egel-Matani describes a *S. cerevisiae* YAP3, and YAP3 type protease has been deleted from the claims. Furthermore, there is no reasonable expectation of success because the effects of deletion of a gene in one species will not necessarily correlate to another species.

Applicant's traversal has been fully considered and found to be persuasive in that Egel-Matani teaches a *S. cerevisiae* YAP3, which has been deleted. However, the Examiner is arguing that there is a reasonable expectation of success, see below. The 35 USC §102(b) rejection is withdrawn. However, applicants' amendment has necessitated the new grounds of rejection under 35 U.S.C. 103(a) recited below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 14, 15, 17-21 and 23-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,110,703 (Egel-Matani) in view of the *Schizosaccharomyces pombe* genome database, and in further view of Hombergh et al. This rejection is necessitated by amendment.

Egel-Matani et al teach a method of constructing a transformed eukaryotic microorganism for the production of a heterologous polypeptide wherein the host comprises an inactive Yap3 protease which prevents the degradation of the heterologously produced protein (see entire document, especially column 19, claim 1; column 20, claim 11; as well as columns 10-12, Examples 6-10). Egel-Matani et al teach such a method wherein the eukaryotic host microorganism is *S. pombe* (see, e.g., column 4, lines 7-12; and column 20, claim 11). Egel-Matani et al further teach that inactivation of Yap3 results in 2-fold higher production of the polypeptide than would occur in yeast with wild-type levels of Yap3 protease activity (column 19, claim 1). Egel-Matani et al also teach the collection/isolation of the heterologous protein (ibid).

However it does not teach deleting the *S. pombe* proteases, SPAC4F8.07c, SPAC4A8.04, SPAC4F10.02 or SPBC16G5.09 for use in the above method.

The *Schizosaccharomyces pombe* genome database (www.genedb.org/genedb/pombe/) teaches *S. pombe* proteases, SPAC4F8.07c,

SPAC4A8.04, SPAC4F10.02 or SPBC16G5.09. As evidenced by Wood et al (Nature 415: 871-880, 2002), these proteases were part of the genome sequencing project published on February 21, 2002. Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Hombergh et al (Tibtech 15: 256-263, 1997, specifically p. 256) teach that heterologous protein production can be improved by eliminating specific protease activities in fungi. Homologous and heterologous protein production by filamentous fungi is often limited by the expression of proteases at high levels. Both classical mutagenesis and gene disruption techniques have yielded strains with reduced protease expression.

The method of constructing a *S. pombe* yeast cell, with a deleted protease gene, for the production of heterologous proteins was known. *S. pombe* proteases, SPAC4F8.07c, SPAC4A8.04, SPAC4F10.02 or SPBC16G5.09 were known. It was also known that deleting endogenous proteases could improve heterologous protein production. Therefore, it would have been obvious to delete or inactivate any of the *S. pombe* protease genes claimed to improve protein production. All of the genes recited in the claims are proteases. They are listed in the alternative and are interchangeable for the purpose of improving heterologous protein production. It would have been obvious to one of ordinary skill in the art to substitute one protease for another to achieve the predictable result of improving heterologous protein production. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the

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applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 14 and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3 and 4 of copending Application No. 12/025,138. Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 1 of copending Application No. 12/025,138 claims a method of constructing an improved *S. pombe* host for expression of a recombinantly introduced foreign gene by deleting or inactivating an

endogenous gene, wherein the endogenous gene is a serine protease is the same method in claim 14 of the instant application, except that in the instant application the serine protease is *S. pombe* isp6. Claim 3 of copending Application No. 12/025,138 claims a method of constructing an improved *S. pombe* host for expression of a recombinantly introduced foreign gene by deleting or inactivating two or more endogenous genes, wherein the endogenous gene is a serine protease and a metalloprotease, for example, and is the same method in claim 20 of the instant application, except that in the instant application the serine protease is *S. pombe* isp6, and the metalloprotease is SPCC865.04c. Since the instant application claims one or more genes, it would be obvious to use 2 or 3 genes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 14 and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2 and 5 of copending Application No. 12/025,138 in view of www.genedb.org/genedb/pombe/, and in further view of Hombergh et al.

Claim 2 of copending Application No. 12/025,138 claims a method of constructing an improved *S. pombe* host for expression of a recombinantly introduced foreign gene by deleting or inactivating an endogenous gene, wherein the endogenous gene is SPAC1006.01, SPAC1296.03c, SPA22G7 or SPBC18A7.01, and is the same as the method in claim 14 of the instant application, except that in the instant application

the serine protease is *S. pombe* isp6. Claim 5 of copending Application No. 12/025,138 claims a method of constructing an improved *S. pombe* host for expression of a recombinantly introduced foreign gene by deleting or inactivating three endogenous genes wherein two of the endogenous genes are a serine protease (isp6, SPBC1711.12, SPAC1006.01 or SPAC1296.03c), and one gene is a metalloprotease (SPAC23H4.09, SPBC14C8.03 or SPAP14E8.04), for example, and is the same method in claim 20 of the instant application, except that in the instant application the serine protease is only *S. pombe* isp6, and the metalloprotease is SPCC865.04c. Since the instant application claims one or more genes, it would be obvious to use 2 or 3 genes.

The method of constructing a *S. pombe* yeast cell, with a deleted protease gene, for the production of heterologous proteins was known. *S. pombe* proteases, SPAC4F8.07c, SPAC4A8.04, SPAC4F10.02 or SPBC16G5.09 were known. It was also known that deleting endogenous proteases could improve heterologous protein production. Therefore, it would have been obvious to delete or inactivate any of the *S. pombe* protease genes claimed to improve protein production. All of the genes recited in the claims are proteases. They are listed in the alternative and are interchangeable for the purpose of improving heterologous protein production. It would have been obvious to one of ordinary skill in the art to substitute one protease for another to achieve the predictable result of improving heterologous protein production. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said

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skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

This is a provisional obviousness-type double patenting rejection.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE K. JOIKE whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Weitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michele K Joiike, Ph.D./

Michele K Joiike, Ph.D.
Examiner
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